Table 1. Correlation between laboratory parameters and categorical outcomes

Parameter (units) median, [range]	CRP (mg/L)	C3 (mg/dL)	(mg/dL)	IgG (mg/dL)	HGB (g/dL)	Lymph (K/uL)	Platelets (K/uL)
Intensity of immunosuppression							
none/mild (n=49)	0.73 [0.3-44]	129 [66-179]	24 [15-37]	887 [200-3380]	13.3 [10.7-17.1]	1.63 [0.34-7.55]	n.s.*
moderate (n=71)	0.69 [0.15-41.6]	128 [64-210]	27 [13-61]	570 [98-2190]	12.5 [8.2-16.1]	1.22 [0.11-5.00]	n.s.
high (n=69)	1.22 [0.3-58.9]	147 [76-216]	31 [13-74]	580 [142-2050]	12.3 [8.9-16.2]	1.00 [0.15-5.30]	n.s.
p-value	0.008	0.0046	0.0011	0.002	0.0006	0.011	
Activity by therapeutic intent							
non active (n=84)	0.61 [0.15-44.3]	126 [64-210]	24 [13-74]	n.s.	n.s.	n.s.	223 [33-465]
active (n=71)	1.73 [0.3-58.9]	145 [76-216]	31 [15-68]	n.s.	n.s.	n.s.	278 [56-648]
p-value	<0.0001	0.0003	0.0004				0.012
NIH global severity stage							
moderate (n=62)	0.62 [0.15-27]	122 [66-187]	n.s.	n.s.	n.s.	n.s.	214 [33-461]
severe (n=125)	1.15 [0.26-58.9]	139 [64-216]	n.s.	n.s.	n.s.	n.s.	265 [34-648]
p-value	<0.0001	0.0017	n.s.	n.s.	n.s.	n.s.	0.0028

*Not significant.

inflammation and cGvHD severity and activity we analyzed a large prospective patient cohort.

Methods: 189 adults were enrolled onto the NCI cross-sectional cGvHD natural history study between 2004-2010. 33% had moderate and 66% had severe cGvHD per NIH criteria (88% classic, 12% overlap). 80% were receiving systemic immunosuppression and failed a median of 4 (range 0-9) prior therapies (PST). Median follow-up of survivors was 30.3 months (1-70). Laboratory predictors included: CRP, ferritin, complement, albumin, IgG, β-2 microglobulin, total protein, PTH (parathyroid hormone), ESR, CBC and platelets. cGvHD severity outcomes included: NIH global stage (moderate vs. severe), NIH average organ score, Lee symptom scale, SF36 physical scale, Schirmer's tear test, Schubert oral mucositis scale (OMRS), skin body surface area (BSA) as continuous outcomes. cGvHD activity outcomes (categorical) included: intensity of immunosuppression (none/mild, moderate, high), clinician's global assessment (CGA) of change (7-point scale) and active vs. non active based on therapeutic intent at enrollment.

Results: Correlation between continuous outcomes and laboratory parameters was weak. Significant univariate analysis results related to categorical outcomes are shown in the Table. By multivariable logistic regression analysis taking into consideration clinical, demographic and laboratory parameters, lower albumin ($p < 0.0001$), higher platelets ($p = 0.045$) and higher number of PST ($p < 0.0001$) were associated with active disease (identifying 75% of active and 77% of non-active cases). Similarly, higher platelets ($p = 0.021$), higher number of PST ($p < 0.0001$) and lower FEV1 ($p < 0.0001$) were associated with severe disease (identifying 76% of severe and 74% of moderate cases). Only higher absolute lymphocytes ($p = 0.019$), higher IgG ($p = 0.0054$) and lower PTH ($p = 0.045$) were associated with better survival in univariate analysis.

Conclusion: Some common laboratory indicators of inflammation can serve as markers of active and severe cGvHD. Better understanding of biologic mechanisms influencing these markers may lead to deciphering the biology of cGVHD and designing therapeutic approaches.

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EXPRESSION OF THE CHEMOKINE RECEPTOR CCR5 ON BLOOD CD11C+ CD16+ DENDRITIC CELLS POST-ALLOGENEIC HEMOPOIETIC CELL TRANSPLANT IS PREDICTIVE FOR THE DEVELOPMENT OF ACUTE GRAFT VERSUS HOST DISEASE

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Introduction: Dendritic cells (DC) are centrally involved in the development of acute graft-versus-host disease (GvHD) following allogeneic hematopoietic cell transplantation (alloHCT). We previously showed that the activation status, as assessed by CMRF-44 antigen expression, of blood CD11c+ myeloid DC is highly associated with the severity of acute GvHD, and that activated DC may be detected in the circulation prior to clinical presentation of GvHD (Transplantation 2007;83: 839–846). We also reported that there was also a positive correlation between aGVHD and the expression of the chemokine receptor CCR5 on myeloid DC (Blood, 114,Suppl.:2251,2009). Because of the phenotypic and functional heterogeneity of the CD11c+ DC population, we further investigated the precise nature of the CD11c+ DC subset expressing CCR5 in the peripheral blood in 24 patients post alloHCT, and correlated the findings with GVHD outcomes.

Methods: Peripheral blood was collected twice weekly up to day 100 post transplant from 24 alloHCT patients. The expression of CCR5 receptor on CD11c+ and CD11c- DC subsets was evaluated using multiparameter flow cytometry.

Results: Eleven of 24 patients developed acute GvHD (4 grade I, 7 grades II-IV), the remaining 13 patients had no GvHD. The percentage of CD11c++ CD16+ DC expressing CCR5 correlated with the development of acute GvHD grades II-IV. The maximum CCR5 expression detected on CD11c+ CD16+ DC in patients developing grade II-IV GvHD (mean 36.0 +/− 6.9%, n = 7)was higher than in those with grade 0-I GvHD (17.2 +/− 3.2 %, n = 17) ($p = 0.0153$), and occurred prior to the clinical onset of GVHD in 6 of 8 patients with CCR5 levels > 20%. Levels of expression of CCR5 on other DC subsets, including CD16- CD11C+ DC, were not preditive for GVHD.

Conclusion: Expression of CCR5 on circulating CD11c+ CD16+ myeloid DC post allo-HCT correlates with the development of moderate to severe GvHD. This observation may indicate altered homing patterns of these cells during the alloimuune response. Detection of raised numbers of CCR5+ CD11c+ CD16+ DC could allow earlier therapeutic intervention prior to the development of clinical GVHD, if these findings are confirmed in a larger study.

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IMPAIRED THYMOPOIESIS WITH NORMAL T REGULATORY CELL NUMBERS IS ASSOCIATED WITH SEVERE CHRONIC GRAFT-VERSUS-HOST DISEASE

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Chronic GVHD (cGVHD) is a significant complication of allogeneic hematopoietic stem cell transplantation (AHSCT). Although T cells have been implicated in cGVHD pathobiology, the role of the thymus in this process has yet to be defined. We characterized thymus and spleen T cell subsets in a murine model of cGVHD to elucidate the role of the thymus in this process. The murine model of minor-histocompatibility mismatch cGVHD, B10.D2- > BALB/c, was validated by pathologic review that correlated with the clinical scoring and showed cGVHD pathology in skin, stomach,